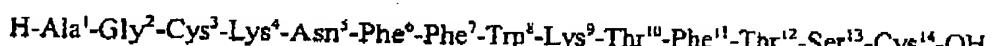


In the Specification:

The paragraph that starts on line 27 of page 1 has been amended to read as follows:

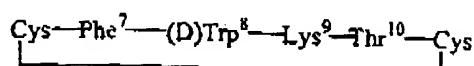
-- Natural somatostatin (also known as Somatotropin Release Inhibiting Factor, SRIF) of the following structure

(SEQ ID NO.: 1)

was first isolated by Guillemin and colleagues (Bruzeau *et al.* Science, 179:78, 1973). It exerts its effect by interacting with a family of receptors. Recently, five receptor subtypes, termed SSTR1 to 5, have been identified and cloned. The precise functional distinction between these receptor subtypes has not yet been fully elucidated --

The paragraph that starts on line 14 of page 2 has been amended to read as follows:

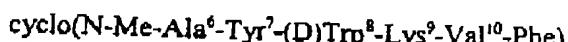
-- Nevertheless, a hexapeptide somatostatin analog containing these four amino acids anchored by a disulfide bridge:

(SEQ ID NO.: 2)

is almost inactive both *in vitro* and *in vivo*, although it has the advantage of the covalent disulfide bridge which replaces the Phe⁶-Phe¹¹ hydrophobic interactions in natural somatostatin. --

The paragraph that starts on line 31 of page 2 has been amended to read as follows:

-- The somatostatin analog, MK-678:

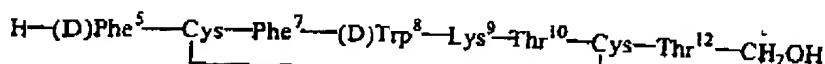
(SEQ ID NO.: 3)

is an example of a highly potent somatostatin analog designed using the first three approaches above (Veber, *et al.*, Life Science, 34:371, 1984). In this hexapeptide analog, a

cis-amide bond is located between N-Me-Ala and Phe¹¹, Tyr⁷ and Val¹⁰ replace Phe⁷ and Thr¹⁰ respectively, and Phe¹¹ is incorporated from natural somatostatin. --

The paragraph that starts on line 3 of page 3 has been amended to read as follows:

-- Another group of somatostatin analogs (U.S. Pat. Nos. 4,310,518 and 4,235,886) includes Octreotide

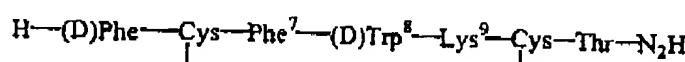


(SEQ ID NO : 4)

the first approved somatostatin analog clinically available and it was developed using the third approach described above. Here, (*D*)Phe⁵ and the reduced C-terminal Thr¹²-CH₂OH are assumed to occupy some of the conformational space available to the natural Phe⁶ and Thr¹², respectively. --

The paragraph that starts on line 11 of page 3 has been amended to read as follows.

-- The compound TT-232.

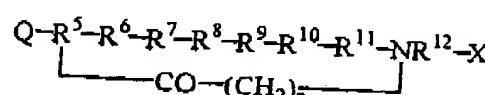


(SEQ ID NO : 5)

is closely related to Octreotide and is an example of implementing the fourth approach described above. The lack of Thr¹⁰ is probably responsible for its high functional selectivity in terms of antitumor activity. --

The paragraph that starts on line 14 of page 17 has been amended to read as follows.

-- One embodiment has the following formula:



(SEQ ID NO : 6)

Formula No 7

wherein m and n are is 1 to 5,

X designates a terminal carboxy acid, amide or alcohol group;

Q is hydrogen or a mono- or di-saccharide;

R⁵ is gamma amino butyric acid, diamino butyric acid, Gly, α-Ala, 5-amino pentanoic acid or amino hexanoic acid;

R⁶ is (D)- or (L)-Phe or Tyr;

R⁷ is (D)- or (L)-Trp, (D)- or (L)-Phe, (D)- or (L)-1Nal, (D)- or (L)-2Nal, or Tyr;

R⁸ is (D)- or (L)-Trp;

R⁹ is (D)- or (L)-Lys,

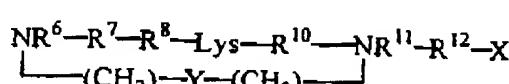
R¹⁰ is Thr, Gly, Abu, Ser, Cys, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R¹¹ is (D)- or (L)-Phe, (D)- or (L)-Ala, Nle, or Cys, and

R¹² is Gly, Val, Leu, (D)- or (L)-Phe, 1Nal, or 2Nal; --

The paragraph that starts on line 14 of page 19 has been amended to read as follows.

-- Yet another embodiment has the general formula:



(SEQ ID NO : 7)

Formula No 9

wherein m and n are 1 to 5;

X designates a terminal carboxy acid, amide or alcohol group;

R⁶ is (D)- or (L)-Phe, or (D)- or (L)-Ala;

R⁷ is Tyr or (D)- or (L)-Phe;

R⁸ is (D)- or (L)-Trp, (D)- or (L)-1Nal, or (D)- or (L)-2Nal,

R¹⁰ is Thr, Val, Ser, or Cys;

R¹¹ is Gly or (D) or (L)-Phe;

R¹² is Thr, GABA, (D)- or (L)-1Nal, (D)- or (L)-2Nal, or (D) or (L)-Phe; and

Y² is amide, thioether, thioester or disulfide

Preferably,

R⁶ is (D)- or (L)-Phe;

R⁷ is Tyr;

R⁸ is (D)Trp, (D)1Nal, or (D) 2Nal;

R¹⁰ is Val;

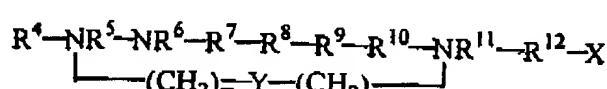
R¹¹ is Gly;

R^{12} is Thr, 1Nal, 2Nal; and

Y^2 is amide. --

The paragraph that starts on line 1 of page 20 has been amended to read as follows:

-- One more preferred embodiment has the following formula.



(SEQ ID NO.: 8)

Formula No 10

wherein m and n are 1 to 5,

X designates a terminal carboxy acid, amide or alcohol group,

R^4 is absent or is a terminal group of one to four amino acids;

R^5 is 1Nal, 2Nal, .beta.-Asp (Ind), Gly, Tyr, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^6 and R^7 may be absent, or are independently Gly, Tyr, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^8 is (D)- or (L)-Trp,

R^9 is (D)- or (L)-Lys;

R^{10} is absent or is Gly, Abu, Cys, Thr, Val, (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^{11} is Cys, (D)- or (L)-Ala, or (D)- or (L)-Phe,

R^{12} is absent or is Val, Thr, 1Nal or 2Nal; and

Y^2 is amide, thioether, thioester or disulfide.

Preferably:

R^4 is absent;

R^5 is (D)- or (L)-Phe, or (D)- or (L)-Ala;

R^6 may be absent and R^7 , when present, and R^8 are independently (D)- or (L)-Phe, Ala or Tyr,

R^{10} is absent or is Thr, Val or (D)- or (L)-Phe,

R^{11} is (D)- or (L)-Ala, or (D)- or (L)-Phe, and

R^{12} is absent.

Alternatively:

R^5 is (D)- or (L)-Ala, or (D)- or (L)-Phe;

R^6 is absent or is (D)- or (L)-Ala, or (D)- or (L)-Phe,

R^7 is (D)- or (L)-Ala, or (D)- or (L)-Phe;

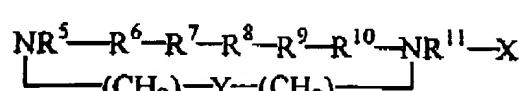
R^{10} is absent or is Thr, Cys, (D)- or (L)-Ala;

R^{11} is Cys, (D)- or (L)-Ala, or (D)- or (L)-Phe; and

R^{12} is absent or is Thr --

The paragraph that starts on line 35 of page 20 has been amended to read as follows:

-- Another embodiment has the general formula:



(SEQ ID NO. 9)

Formula No. 11

wherein: m and n are 1 to 5;

R^5 is (L)- or (D)-Phe, Tyr or (D)- or (L)-Ala;

R^6 is (L)- or (D)-Phe, Tyr or (D)- or (L)-Ala;

R^7 is absent or is (D)- or (L)-Phe, Tyr, or (D)- or (L)-Ala,

R^8 is (D)- or (L)-Trp;

R^9 is (D)- or (L)-Lys;

R^{10} is absent or is Thr, Val, Cys or (D)- or (L)-Ala,

R^{11} is (L)- or (D)-Phe, Cys, (D)- or (L)-Ala;

Y^2 is amide, thioether, thioester or disulfide.

Preferably:

R^5 is (D)- or (L)-Ala;

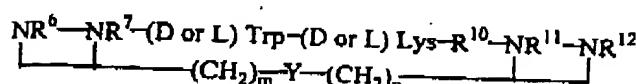
R^7 is absent or is (D)- or (L)-Phe;

R^{10} is Thr;

R^{11} is Cys; and

X is an alcohol group --

The paragraph that starts on line 21 of page 21 has been amended to read as follows.
--Yet another embodiment has the general formula



(SEQ ID NO.: 10)

Formula No 12

wherein:

the dotted line indicates that the bridge is connected to NR⁶ or NR⁷ at one end and to NR¹¹ or NR¹² at the other end;

R⁶ is absent or is (D)- or (L)-Phe or Ala,

R⁷ is (D)- or (L)-Phe, Ala or Tyr;

R⁸ is Thr, Ala, Val or Cys;

R¹¹ is absent or is (D)- or (L)-Phe, Ala or Cys;

R¹² is absent or is Thr or Thr reduced to an alcohol; and

Y³ is amide, thioether, thioester or disulfide

Preferably, the bridge is connected to NR⁶ and NR¹¹ or to NR⁶ and NR¹² with R¹² being Thr reduced to an alcohol --